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AN EXPERIMENTAL TEST OF THE COMBINED EFFECT OF QUARTZ DUST AND RADON

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/Following is the translation of an article by V. S. Kushneva entitled "Kombinirovannoye Deystviey Kvartsevoy Pyli i Radona v Eksperimente (English version above) in Gigiyena Truda i Professional'nyye Zabolevaniya, Vol. 4, No. 1, Moscow, 1959, Pages 22-28./

There is a scarcity of material in the literature dealing with the question of the temporary effect on the organism of quartz dust and radioactive substances. A matter of particular interest is the study of the combined effect upon an organism of quartz dust and radon, which are continually present in the atmosphere of uranium and radium mines.

The literature which was available to us on the morbidity of workers in uranium and radium mines pertains principally to the mountainous areas of Shneyeberg and Ioakhimstal and is devoted primarily to bronchogenic carcinoma, a disease specific for these regions.

The majority of investigators recognize the occupational factor in the development of lung cancer among the workers from these mines and consider radioactivity to be the principal carcinogen, in particular, the inhalation of even small amounts of radium emanation (Osikl, Shraub, Rajewsky, Lange, Behounek, Ludewig and Lorenser).

The majority of the investigators have not devoted sufficient attention to the frequency of silicosis among the miners, nor to the character of its course. At the same time the high levels of silicon dioxide in these mines unarguably attests to the fact that silicosis represents a real threat. A number of authors (Roxtoski, Saupe, Schmorl), turning their attention to the silicosis morbidity among this group of workers, detected far-advanced pneumoconiosis among the majority of miners examined. Ziel found that 60% of the miners had pneumoconiosis of the lungs and 90% had a catarrhal disorder of the upper respiratory tract.

In 1939, as part of a mass roentgenologic survey of miners who had worked in mines not less than 10 years, Saupe discovered silicosis in 172 of 398 individuals surveyed; in 32 there was silicosis of stages II and III.

A pronounced nodular form of silicosis was rarely encountered, but in individual cases there was an atypical distribution of silocotic nodules.

The present experimental investigation was undertaken to elucidate the combined effect of radon and silicon dioxide on the animal organism.

Method of Investigation

The experimental work was performed as a comparitive study of the combined effect of quartz dust and radon as well as the effect of each of them individually on four groups of animals (white rats) with about 30 in each group.

The animals of group I were subjected to the effect of a fine dispersion of quartz dust, those of group II to the effect of radon, those of group III to the combined action of quartz dust and radon; group IV was a control group and was kept under the same conditions as the animals of the first three but without exposure to the test substances. A single dose of 50 mg of quartz-containing dust was delivered into the tracheas of each animal in groups I and III. Radon intoxication of the animals of groups II and III was accomplished by static inhalation in a hermetic chamber at a concentration of 8×10^{-6} C/l for triple exposures of an hour each.

In addition, another group (group B) of animals (12 white rats) was subjected to the combined effect of dust and radon at the same concentrations as the animals in group III, but the action of the radon was more prolonged -- about 2 hours twice a week for a period of 2 months (total combined exposure of 18 hours). The radon intoxication was begun the day after exposure to quartz dust.

Regular and dynamic observation of all of the animals was performed. Studied were their clinical states, survival, shifts in peripheral-blood composition and pathological organ changes. With the development of pathological processes the animals were sacrified after a specified interval, equal to all four groups, and subjected to pathological study. Autopsy and microscopic examination was also performed on the animals which succumbed. The overall duration of the observations of the animals lasted approximately 2 years. (The work was performed under the direction of Professor E. B. Kurlyandskaya).

Observation of the animals in group III, subjected to the combined effect of quartz-containing dust and radon, showed that the mortality of the rats over a 10-month period was 34%. Among the animals subjected to the combined action

of the dust and more prolonged radon intoxication (totalling 18 hours) the mortality was even higher, amounting to 90% for the same period of observation. The mortality was lower among the animals subjected to the separate effects of dust and radon.

An increase in body weight was noted among all the experimental animals for the period of observation. In approximately half of the animals of groups II (dust and radon) and II (radon), there was a slight rapid fall in body weight after the intoxication, followed by recovery. The weight gain of the animals subjected to the combined action was less than the gain of the animals in the first two groups and amounted to only 40% as compared with gains of 72 and 55 % in the first two groups.

Examination of the composition of the peripheral blood also showed the greatest changes in the group of animals subjected to the combined effect of dust and radon: intermittent fluctuations in erythrocyte and hemoglobin levels were noted, as well as an elevation in the reticulocyte count immediately after intoxication.

For the extent of the entire period of observation a sharp rise was noted in the white cell count, which in a number of cases reached a level of 28,000 to32,000 (principally through an elevation of lymphocyte levels; in a number of cases a neutrophilic leukocytosis was noted, evidently caused by inflammatory processes in the lungs, which were frequently seen in animals of this group).

The changes in the composition of the peripheral blood were associated with the action of radon on the animal organism which had been exposed to the effects of dust.

The blood picture of the animals (Group B) which, in addition to dust, had been subjected to more prolonged exposure to radon than the animals of group III (a total of 18 hours) was of the same nature as that detected among the animals of group III, but all the changes were more pronounced. The two animals of this group which had perished soon after exposure to dust and radon showed a sudden depression of both erythropoiesis and thrombopoiesis, and in a single animal of leukopoiesis as well.

This animal's erythrocyte count fell to 3,700,000, hemoglobin level to 62%, reticulocyte count to 1,5/1000 platelets to 139,000, leukocytes to 3000 and lymphocytes to 1860.

The animal succumbed with a hyperchromic anemia, reticulopenia, thrombopenia, leukopenia and lymphopenia.

The data presented show that the changes in the picture of the peripheral blood were undoubtedly occasioned

by the effect of radon on the experimental animals. This notion is in agreement with the data in the literature on the effect of other radioactive substances on the hematopoietic function of the organism (A. P. Yegorov et al.).

A study of the pathomorphologic changes (performed with the consultation of Professor P. P. Dvishkova) and, in particular, a comparison of the pathological findings in the animals subjected to the combined effect of dust and radon (group III) and those exposed to dust along (group I) showed a substantial difference in the course of pathological processes, especially in the lungs.

Experimental silicosis in a form typical for white rats which has been described by many authors (E. N. Gorodenskaya, P. P. Dvishkov et al.) developed in animals of group I after exposure to quartz dust. This was characterized by the appearance of miliary and submiliary nodules composed of epithelioid and histiocytic elements. The nodules were sharply delimited peripherally from the surrounding, practically unaltered pulmonary tissue, because of a tendency of the fibers located in the boundary layer to form circular whirls. In later periods individual nodules converged and formed areas of fibrous tissue.

In a number of cases there was moderate thickening of intralveolar walls with connective tissue growth along bronchi and vessels.

The pathological process in the lungs of animals of group II (dust and radon) was also of the silicotic type, but was of a more intensive and diffuse nature. In this series of observations, even in the early periods, the formation of numerous large nodules was observed, frequently converging and forming large areas of a specific tissue (Figure 1). The nodules, which were composed of dust cells, lymphoid cells and surrounding connective-tissue cells, grew in a reticulum of fibrous connective tissue. These foci, however, were not sharply delimited from the boundaries of the surrounding tissue, as is distinctly typical for silicotic nodules, and the cellular elements in the foci lacked the characteristic concentric distribution.

Along with the nodular fibrosis a diffuse infiltrative-proliferative process was noted among all the animals of this group in the intralveolar walls and in the peribronchial and perivascular spaces. In individual cases one could see compressed alveolar lumina among the thickened, sclerosed walls; in other cases the process had led to such marked thickening of the intralveolar walls that the alveolar lumina had completely disappeared.

An accumulation of lymphoid elements was noted in the peribronchial and perivascular areas, as well as marked hyperplasia of peribronchial follicles.

Among the animals of group III (dust and radon) a severe desquamation of the alveolar epithelium was also noted, not only immediately after the exposure to dust, but even 4 to 5 months after intoxication. Fine fatty droplets were frequently noted in the sloughed cells of the alveolar epithelium.

Typical of the animals in group III (dust and radon) were bronchial changes in the form of bronchitis (desquamative, purulent, etc.), peribronchitis, panbronchitis with complete dastruction of the wall, as well as peribronchial sclerosis leading eventually to deformation of the walls and the development of bronchoectasia.

In the same grop of animals attention is merited by characteristic changes in the bronchial epithelium, which altered its form and dimensions. Initially the bronchial epithelium was unusually tall; at later stages a thickening was noted with a transformation into stratified cuboidal and finally into stratified squamous epithelium. The appearance of adenomatous overgrowth was noted. In one rat, which perished 1½ years after combined exposure to dust and radon, a malignant neoplasm was detected -- a solid adenocarcinoma, apparently arisi from the bronchi (Figure 2). Cancerous nodes were detected not only in the lung parenchyma, but were distributed throughout the entire pleural surface, penetrating the mediastinal space.

Among animals sacrified after 9 to 11 months, severe condensation of lung parenchyma was observed as a result of the nodular and massive diffuse overgrowth of connective tissue (Figure 3).

Bone-tissue growth had occurred in the walls of the blood vessels and lung parenchyma in a number of animals sacrificed at later periods (Figure 4).

Inflammatory phenomena (pneumonia, frequently going on to suppuration) were seen in the animals subjected to the combined effect of dust and radon.

Findings in the other internal organs of animals of this group included acute congestion, the deposition of and dark-brown pigment (hemosiderin) in the cells of the reticuloendothelial system and varying degrees of evident degenerative and sclerotic changes, and, in one case, hemorrhage into the muscular wall of the heart.

Histological examination of the lungs of the animals subjected to the effect of radon alone show that it is the radon which accounts for the nature of the silicotic process

observed in the face of the combined action of quartz dust and radon.

Thus the combined effect of quartz dust and radon results in a more severe form of silicosis.

The pathological process produced in the lungs by radon does not subside when the exposure ceases, but continues to develop for a long period of time, with the establishment of severe irreversible long-range sequelae.

It can be supposed that the prolonged course of the pathological process results from the highly injurious effect of radon and its disintegration products on pulmonary tissue.

Actually the lungs are an organ in which radon exerts a double effect -- in inspiration, when it enters the blood from the air, and in expiration, when the gas leaving the blood stream exits along with the expired air.

In addition to the effect on the organism of the radon itself, additional damage is done by the active solid residue (Ra"A", Ra"B", Ra"C", etc.), which is formed in the radioactive disintegration of radon.

We conjectured that pneumoconiosis may favor the retention of solid particles of active residue on the surface of dust particles and itself aggravate the course of the pathological process.

In order to prove this supposition, the following experiment was set up: one group of animals was exposed to quartz dust, and a control group was not. Then both groups were subjected to the effects of radon under identical conditions.

On the day following or, more usually, the fourth day after the final exposure to radon, the experimental animals were sacrificed, their lungs combusted and the activity of the salts determined by means of an end-type counter on a B-2 apparatus.

These determinations showed that among those animals subjected to prior dust exposure the activity of the salts (in counts per second) was higher (by approximately 5 to 10 times) than the activity of the salts of the lungs which did not contain the dust. Apparently molecular residues of the products of radon disintegration are deposited on the dust particles in the lungs. The adsorbed particles, which consist of solid radioactive daughter substances, have a deleterious effect upon the organism.

Apparently a similar process is in operation in the air within mines, where the molecular particles of solid active residue remain suspended inthe air for a long time and can be deposited on dust particles and enter the human

organism with the inspired air.

CONCLUSIONS

1. The combined effect of quartz dust and radon in concentrations of 8.10^{-6} C/L in three one-hour exposures results in an increased mortality, a slight decrease in the animals' body weight immediately after the exposure and an overall reduction in weight gain as compared with exposure to each of these factors separately.

2. In the peripheral blood of the experimental animals fluctuations were detected in the level of formed elements, as well as a rise in reticulocytes immediately after the radon exposure and leukocytosis, resulting from an increase in the number of lymphocytes. Depression of hematopoiesis was observed in some of the animals when the radon exposure was increased.

3. The pathological process arising in the lungs as a result of the combined action of quartz dust and radon is silicotic in nature, but of more severe and prolonged character, produces an earlier and severe involvement of the bronchi, marked desquamation and is frequently associated with secondary infection. Hyperemia is seen in the parenchymatous organs, and occasionally hemorrhagic, degenerative, inflammatory as well as sclerotic phenomena.

4. Sudden metaplasia of the bronchial epithelium and the growth of neoplasms of heterologous tissue (bone, cancer, etc.), caused by the effect of the radon, were characteristic for the group of animals subjected to the combined effect of dust and radon.

5. The presence of dust particles in the lungs increases the retention of radioactive products of radon disintegration within the lungs, with a resultant increased danger of radiation damage to the organism.

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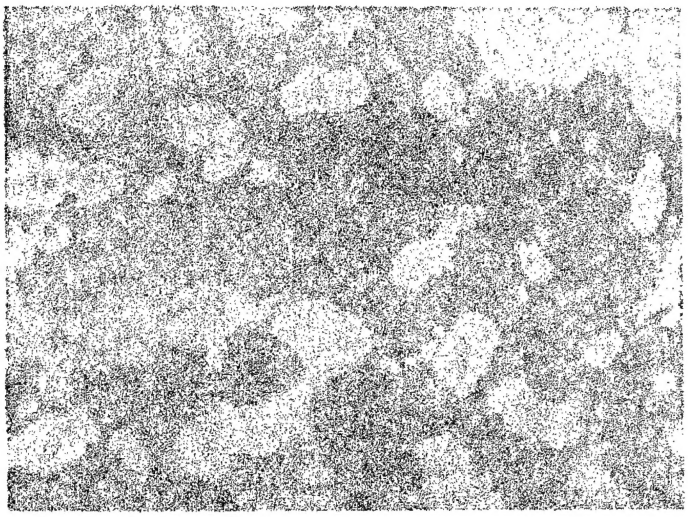

Figure 1. Group II, Rat #23. Sacrificed on the 95th day following exposure. Lungs. Multiple miliary silicotic nodules.

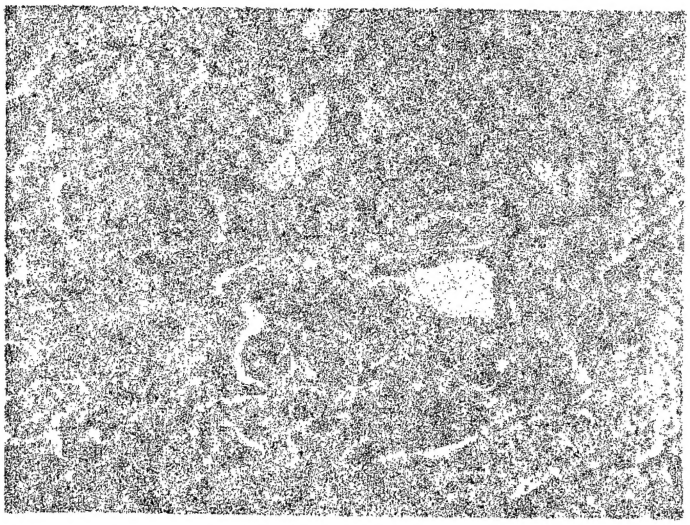

Figure 2. Group III. Rat # 35. Succumbed 1½ years after exposure. Lungs. Adenocarcinoma.

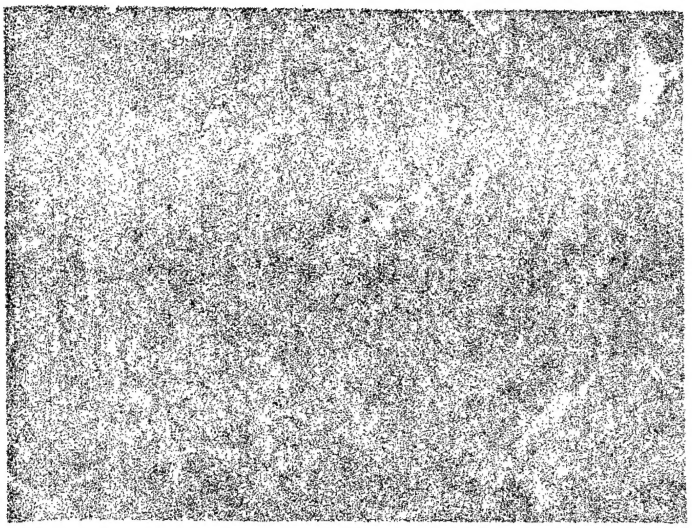

Figure 3. Group III. Rat # 23. Sacrificed on the 95th day following exposure. Lungs. Large Sclerotic areas formed by confluence of silicotic nodules.

Figure 4. Group III. Rat #3. Sacrificed on the 347th day following exposure. Lungs. Bone tissue in the wall of a blood vessel.

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